PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Giorgio MARI et al.	Art Unit: TBD
Early Serial No.: 10/525,044	Examiner: TBD
Filed: February 18, 2005	Atty. Docket: P70417US0

Title: FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS

RENEWED PETITION UNDER 37 C.F.R. §1.47

MAIL STOP PCT
Commissioner for Patents
Office of PCT Legal Adminstration
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants, through their undersigned attorney, hereby submit a renewed Petition under 37 C.F.R. §1.47 requesting waiver of the requirement of 37 C.F.R. §1.64 that each of the actual inventors execute the oath or declaration. For the reasons set forth herein, an extraordinary situation is presented and justice requires that signature of the declaration by each of the inventors be waived.

Applicants submitted an original Petition August 1, 2005. On November 14, 2005, Applicants' Petition was dismissed because (1) the Petition did not include evidence that the nonsigning inventor, Dr. Ori, was presented with both a declaration/power of attorney form and a copy of the complete application, including the specification, drawings and claims, and (2) Applicants failed to provide a statement of facts by the person who presented the inventor with the application papers and/or to whom the refusal was made. A copy of the decision is enclosed with this petition as Exhibit A.

Applicants asked their Italian counsel to again present Dr. Ori with the application papers including the specification, drawings and claims, and document her refusal by the individual who presented the papers to Dr. Ori and to whom the refusal was made. The required facts are as follows:

In this case, one of the original inventors, Dr. Alessandra Ori, has refused to execute a Declaration identifying herself as an inventor.

This application was originally filed identifying inventors Dr. Giorgio Mari , Dr. Paolo Verri and Dr. Alessandra Ori as the inventors. The application was accompanied by a Declaration and Power of Attorney signed by the inventors Mari and Verri, executed on February 10, 2005. A copy of the Declaration and Power of Attorney (the "Declaration") is attached as Petition Exhibit B.

An Assignment wherein each of Drs.. Mari and Verri assigned their entire rights in the application and invention to assignee, Fresenius Hemocare Italia S.r.l., is attached as Petition Exhibit C.

Filed separately herewith as Petition Exhibit D, is a copy of a letter sent to Dr. Ori by registered mail, dated January 5, 2006. The letter indicates that a complete copy of the U.S. patent application, together with the Declaration and Assignment forms, was enclosed and includes a request for Dr. Ori to execute the Declaration and Assignment forms, in Italian. An English translation of the letter to Dr. Ori, as well as a copy of the delivery receipt in Italian, with an English translation are included.

Filed separately herewith as Petition Exhibit E, is a copy of a letter in Italian, from Dr. Ori, dated February 14, 2006, indicating her refusal to execute the application papers and enclosed copies of the application papers mailed to her on January 5, 2006, and an English translation of Dr. Ori's letter.

Filed separately herewith as Petition Exhibit F, are two letters from Mr. Paolo Rambelli, Italian patent counsel for the Assignee. The first letter, dated February 23, 2006 contains a statement

of facts that he received the February 14, 2006 letter from Dr. Ori (Exhibit E) indicating her refusal to sign the application papers and returning same on February 20, 2006. The second letter from Mr. Rambelli is a cover letter to the undersigned attorney enclosing Dr. Ori's letter of February 14, 2006.

The last known address of the non-signing inventor, Dr. Ori, is Via Quattro Ville, 251/1 - 41010 Modena, ITALY as indicated on her letter of February 14, 2006 (Exhibit E).

For the reasons set forth above, it is respectfully requested that this Renewed Petition be granted and that Dr. Ori's signing of the Declaration be waived. A petition fee in the amount of $200.00 was previously paid. Applicants additionally enclose a petition for a two-month extension of time. If the amount provided is incorrect or if the Form PTO-2038 becomes detached, the Director is hereby authorized to charge the required fee, any additional fees, or credit any overpayments, to Deposit Account No. 06-1358.

Respectfully submitted,

JACOBSON HOLMAN, PLLC

By _____

Joseph G. Contrera
Reg. No. 44,628

400 Seventh Street, N.W.
Washington, D.C. 20004-2201
(202) 638-6666
Date: March 6, 2006
HBJ/JGC/gm
R:\SHARED\JGC\P70417US0 Renewed Petition for Nonsigning inventor.wpd

NPO 11/16/05 +1BS P70417US0

14 NOV 2005

UNITED STATES PATENT AND TRADEMARK OFFICE

TC 1648-05

JACOBSON HOLMAN PLLC
Response Due On Or Before
1 / 14 / 06
Month Day Year

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United States Patent and Trademark Office
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Alexandria, VA 22313-1450
www.uspto.gov

OTRE IAP40 MAR 06 2006 PATENT & TRADEMARK OFFICE

JACOBSON HOLMAN, PLLC
400 Seventh Street, NW
Suite 600
Washington, DC 20004

In re Application of:
MARI, Giorgio, et al.
U.S. Application No.: 10/525,044
PCT No.: PCT/EP03/09174
International Filing Date: 19 August 2003
Priority Date: 21 August 2002
Attorney's Docket No.: P70417US0
For: FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS

DECISION ON PETITION UNDER 37 CFR 1.47(a)

This decision is issued in response to applicants' 01 August 2005 petition under 37 CFR 1.47(a). Applicants submitted $130 as the petition fee; the correct petition fee is $200. Deposit Account No. 06-1358 will be charged the remaining $70.

BACKGROUND

On 19 August 2003, applicants filed international application PCT/EP03/09174 which claimed a priority date of 21 August 2002 and which designated the United States. On 04 March 2004, a copy of the international application was communicated to the United States Patent And Trademark Office (USPTO) by the International Bureau (IB). The deadline for submission of the basic national fee was thirty months from the priority date, i.e., 21 February 2005.

On 18 February 2005, applicants filed a transmittal letter for entry into the national stage in the United States accompanied by, among other materials, payment of the basic national fee.

On 07 July 2005, the United States Designated/Elected Office (DO/EO/US) mailed a "Notification Of Missing Requirements" (Form PCT/DO/EO/905) indicating that an oath or declaration in compliance with 37 CFR 1.497 was required.

On 01 August 2005, applicants filed a response to the Notification Of Missing Requirements that included a declaration executed by two of the three inventors, and the petition under 37 CFR 1.47(a) considered herein. The petition requests acceptance of the declaration without the signature of the remaining inventor, Alessandra ORI, whom applicants assert has refused to execute the present application.

DISCUSSION

A grantable petition under 37 CFR 1.47(a) must be accompanied by: (1) the fee under 37 CFR 1.17; (2) a statement of the last known address of the non-signing inventor; (3) an oath or declaration by the other inventors on behalf of themselves and the non-signing inventor; and (4) factual proof that the inventor refuses to execute the application or cannot be reached after diligent effort.

The petition here was accompanied by partial payment of the petition fee, and the authorization to charge Deposit Account No. 06-1358 for additional fees, and it includes a statement of the nonsigning inventor's last known address. Items (1) and (2) are therefore satisfied.

Regarding item (3), section 409.03(a) of the Manual of Patent Examining Procedure ("MPEP") states that:

> An oath or declaration signed by all the available joint inventors with the signature block of the nonsigning inventor(s) left blank may be treated as having been signed by all the available joint inventors on behalf of the nonsigning inventor(s), unless otherwise indicated.

Here, applicants have filed a declaration executed by two of the three inventors and including an unsigned signature box identifying the nonsigning inventor (Alessandra ORI). This declaration is treated as having been executed by the available inventors on their behalf and on behalf of the nonsigning inventor. Item (3) is therefore satisfied.

Regarding item (4), applicants assert that the nonsigning inventor has refused to execute the application. However, before a refusal to execute the application can be claimed, MPEP § 409.03(d) requires that the nonsigning inventor be provided with a copy of the complete application, including specification, drawings, and claims. The MPEP also requires "a statement of facts by the person who presented the inventor with the application papers and/or to whom the refusal was made." Applicants here have supplied a statement from Joseph G. CONTRERA, with accompanying exhibits, as evidence that the inventor has refused to sign the application. However, this statement and the attached correspondence refer only to a copy of the Declaration and Assignment forms being sent to the inventor; there is no evidence that the nonsigning inventor has been provided with a copy of the complete application, as required by the MPEP. In addition, Mr. CONTRERA is not the person who sent the attached correspondence to the nonsigning inventor and to whom the inventor's response was sent. Accordingly, applicant has not provided the required "statement of facts by the person who presented the inventor with the application papers and/or to whom the refusal was made."

Based on the above, item (4) is not satisfied on the present record.

CONCLUSION

The petition under 37 CFR 1.47(a) is **DISMISSED WITHOUT PREJUDICE**.

If reconsideration on the merits of this petition is desired, a proper response must be filed within **TWO (2) MONTHS** from the mail date of this decision. Any reconsideration request should include a cover letter entitled "Renewed Petition Under 37 CFR 1.47(a)" and must be accompanied by the materials needed to satisfy the outstanding requirement for a grantable petition, that is, firsthand evidence that the nonsigning inventor has been provided with a copy of the complete application and has refused to sign the required documents. Such evidence must be provided in compliance with MPEP § 409.03(d).

No additional petition fee is required.

Extensions of time may be obtained under 37 CFR 1.136(a).

Any further correspondence with respect to this matter should be addressed to the Mail Stop PCT, Commissioner for Patents, Office of PCT Legal Administration, P.O. Box 1450, Alexandria, Virginia 22313-1450, with the contents of the letter marked to the attention of the Office of PCT Legal Administration.

Richard M. Ross
PCT Petitions Attorney
Office Of PCT Legal Administration
Telephone: (571) 272-3296
Facsimile: (571) 273-0459

- DECLARATION AND POWER OF ATTORNEY U.S.A.

ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION;
NON PRIORITY; OR PROVISIONAL APPLICATIONS

FOR ATTORNEYS' USE ONLY

ATTORNEYS' DOCKET NO.

101 As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

"Filter for the depletion of leukocytes from blood products"

102 the specification of which:

☐ is attached hereto OR ☒ was filed on: August 19, 2003 as United States Application Number or PCT International application Serial No. PCT/EP2003/009174 and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) or (f), or 365(b) of any foreign application(s) for patent or inventor's or plant breeder's rights certificate, or under 35 U.S.C. 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's or plant breeder's rights certificate(s) having a filing date before that of the application on which priority is claimed:

103

Prior Foreign Application(s) (Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed Yes	No
T02002A000736	Italy	21/08/2002	☒	☐
			☐	☐
			☐	☐

104 I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105 I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status: patented, pending, abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith. HARVEY B. JACOBSON, JR. (20,851); JOHN CLARKE HOLMAN (22,769); ALLEN S. MELSER (27,215); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007); WILLIAM E. PLAYER (31,409); YOON S. HAM (45,307); LINDA J. SHAPIRO (28,264); SUZIN C. BAILEY (40,495); SUZANNAH K. SUNDBY (43,172); MARVIN R. STERN (20,640); AND NATHANIEL A. HUMPHRIES (22,772)

SEND CORRESPONDENCE TO: CUSTOMER NO. 00136 or	DIRECT TELEPHONE CALLS TO: (please use Attorney's Docket No.) (202) 638-6666
JACOBSON HOLMAN PROFESSIONAL LIMITED LIABILITY COMPANY 400 SEVENTH STREET, N.W. WASHINGTON, D.C. 20004	JACOBSON HOLMAN PROFESSIONAL LIMITED LIABILITY COMPANY

*Inventor(s) name must include at least one unabbreviated first or middle name.

201	FULL NAME * OF INVENTOR	FAMILY NAME: MARI	GIVEN NAME: Giorgio	MIDDLE NAME:		
	RESIDENCE & CITIZENSHIP	CITY: MIRANDOLA (Modena)	STATE OR FOREIGN COUNTRY: Italy	COUNTRY OF CITIZENSHIP: Italy		
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Via Genova 1	CITY: MIRANDOLA (Modena)	STATE OR COUNTRY: Italy	ZIP CODE: I-41037	
202	FULL NAME * OF INVENTOR	FAMILY NAME: VERRI	GIVEN NAME: Paolo	MIDDLE NAME:		
	RESIDENCE & CITIZENSHIP	CITY: MIRANDOLA (Modena)	STATE OR FOREIGN COUNTRY: Italy	COUNTRY OF CITIZENSHIP: Italy		
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Via Remondi 3	CITY: MIRANDOLA (Modena)	STATE OR COUNTRY: Italy	ZIP CODE: I-41037	
203	FULL NAME * OF INVENTOR	FAMILY NAME: ORI	GIVEN NAME: Alessandra	MIDDLE NAME:		
	RESIDENCE & CITIZENSHIP	CITY: MODENA	STATE OR FOREIGN COUNTRY: Italy	COUNTRY OF CITIZENSHIP: Italy		
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Quattro Ville 251/1	CITY: MODENA	STATE OR COUNTRY: Italy	ZIP CODE: I-41100	

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201*	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
DATE February 10, 2005	DATE February 10, 2005	DATE

☐ Additional inventors are named on separately numbered sheets attached hereto.

UNITED STATES OF AMERICA -- ASSIGNMENT

(1-6) Insert Name of Inventor(s)

-1 Giorgio MARI

-2 Paolo VERRI

-3 Alessandra ORI

-4

-5 and

-6

In consideration of the sum of one dollar ($1.00), and other good and valuable considerations paid to each of the undersigned, the receipt and sufficiency of which are hereby acknowledged, the undersigned agree(s) to assign, transfer and set over to

-7 Insert Name of Assignee — -7 FRESENIUS HEMOCARE ITALIA S.r.l.

-8 Insert Address of Assignee — -8 of Via Santi 293, I-41032 CAVEZZO (Modena) Italy

-9 Insert Legal Entity and State or Country (e.g., a corporation or citizen of Japan) — -9 a Corporation of Italy

(hereinafter designated as the Assignee) the entire right, title and interest for the United States, its territories, dependencies and possessions, in the invention known as

-10 Insert Identification of Invention, such as Title, Case Number or Foreign Application Number — -10 "Filter for the depletion of leukocytes from blood products"

for which the undersigned has (have) executed an application for patent in the United States of America

-11 Insert Date of signing of Application, or filing date and Serial No., if known — -11 Said application having been executed/filed on _____ (and assigned Serial No. _____

1) The undersigned agree(s) to execute all papers necessary in connection with this application and any continuing or divisional applications and also to execute separate assignments in connection with such applications as the Assignee may deem necessary or expedient.

2) The undersigned agree(s) to execute all papers necessary in connection with any interference which may be declared concerning this or any continuing or divisional applications thereof and to cooperate with the Assignee in every way possible in obtaining evidence and going forward with such interference.

3) The undersigned agree(s) to execute all papers and documents and perform any act which may be necessary in connection with claims or provisions of the International Union for Protection of Industrial Property or similar agreements.

4) The undersigned agree(s) to perform all affirmative acts which may be necessary to obtain a grant of a valid United States patent to the assignee.

5) The undersigned hereby authorize(s) and request(s) the Commissioner of Patents and Trademarks to issue any and all Letters Patents of United States resulting from this application or any continuing or divisional applications thereof to the said Assignee, as Assignee of the entire interest, and hereby covenants that he has (they have) full right to convey the entire interest herein assigned, and that he has (they have) not executed, and will not execute any agreement in conflict herewith.

6) Assignor hereby further assigns to Assignee all claims and causes of action for infringement of the patent rights assigned herein, including the right to sue for, and collect damages for, any and all acts of past and future infringement.

7) The undersigned hereby grant(s) the law firm of **Jacobson Holman PLLC**, 400 Seventh Street, N.W., Washington, D.C. 20004, the power to insert on this assignment any further identification which may be necessary or desirable in order to comply with the rules of the United States Patent and Trademark Office for recordation of this document.

In witness whereof, executed by the undersigned on the date(s) opposite the undersigned name(s).

Date	February 10, 2005	Name of Inventor (typed name)	Giorgio MARI	(SEAL) signature
Date	February 10, 2005	Name of Inventor (typed name)	Paolo VERRI	(SEAL) signature
Date		Name of Inventor (typed name)	Alessandra ORI	(SEAL) signature
Date		Name of Inventor (typed name)		(SEAL) signature
Date		Name of Inventor (typed name)		(SEAL) signature
Date		Name of Inventor (typed name)		(SEAL) signature

This assignment should preferably be signed before a United States Consul if signed abroad, or a Notary Public if domestically signed. If not, then the execution by the inventor(s) should be witnessed by at least two witnesses who sign here:

☐ Additional inventors' names and signatures on a separate sheet.

Witness _____

Witness _____

LAW OFFICES OF
JACOBSON HOLMAN
PROFESSIONAL LIMITED LIABILITY COMPANY
THE JENIFER BUILDING
400 SEVENTH STREET, N.W.
WASHINGTON, D.C. 20004

Guido Jacobacci
Giuseppe Quinterno
Massimo Introvigne
Paolo Rambelli
Fabio Siniscalco
Enrico Riccardino
Patrizia Franceschina
Angelo Gerbino
Gabriele Borasi
Sergio Mulder
Francesco Serra
Silvia Lazzarotto
Carlo Alberto Demichelis

Franca Acuto
Corrado Fioravanti
Edgardo Deambrogi
Giorgio Long
Paolo Ernesto Crippa
Elena Comoglio
Sylvain Rousseau
Ferruccio Postiglione
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Diego Giugni
Lidia Lanza
Davide Rondano
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... Salustri
... Gallo
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Marilena Garis
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Salvatore Pennacchio

Gianluigi Zanettin
Stefania Comisso
Monica Faia
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Maria Antonella Incardona
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Jacobacci & Partners

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TORINO | MILANO | PADOVA | ROMA | BRESCIA | GENEVE | MADRID | ALICANTE

16

- raccomandata a/r -
richiesto avviso di ritorno

DOTT. ALESSANDRA ORI
VIA QUATTRO VILLE 251/1
41100 MODENA MO

Torino, 5 gennaio 2006
Ns. rif.: E053638 - PC451PR (si prega di citare) BEE-fl
Rif. Fresenius: F02/04IT-I08

Domanda di brevetto Internazionale N. PCT/EP2003/009174 del 19 agosto 2003
FRESENIUS HEMOCARE ITALIA SRL
FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS
(ITALIA No. TO2002A000736)

Gentile Dott. Ori,

Facendo seguito alla nostra lettera del 16 febbraio 2005, alla quale allegavamo i documenti di dichiarazione/procura e cessione da farle firmare per completare il deposito della fase nazionale in U.S.A. corrispondente alla suddetta domanda di brevetto Internazionale; e facendo seguito alla sua lettera datata 14 marzo 2005 in cui rifiutava di firmare i suddetti documenti, il nostro agente statunitense ci ha richiesto di spedirle l'allegata copia della domanda completa U.S.A., unitamente ad altri documenti di dichiarazione/procura e cessione.

Le chiediamo nuovamente di rivedere la domanda, di firmare i documenti di dichiarazione/procura e cessione e di restituirceli così da completare il deposito della presente domanda in U.S.A.

Confidiamo in una sua sollecita considerazione in merito a quanto sopra.

Con i migliori saluti,
JACOBACCI & PARTNERS

P. Rambelli

All.: c.s.

Avviso di ricevimento E053´ /PC451PR/BEE/f1

[X] Raccomandata [ ] Pacco

116813102 39 4

Numero

[ ] Assicurata Euro ____

Data di spedizione 10/01/06 Dall'ufficio postale di TORINO

RICEVUTO 02 FEB. 2006

Destinatario DOTT. ALESSANDRA ORI

Via VIA QUATTRO VILLE 251/1

C.A.P. 41100 Località MODENA MO

x DELEGATO

x [signature] x 26-01-06 [signature]

Firma per esteso del ricevente (Nome e Cognome) Data Firma dell'incaricato alla distribuzione

Bollo dell'ufficio di distribuzione

Ed. 02/04 - L3

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Posteitaliane

A. R.

Avviso di ricevimento
Mod. 23-I/0 Cod. W8401E - L3

JACOBACCI & PARTNERS S.p.A.
Corso Emilia n. 8
10152 TORINO

...ngne
...belli
...Siniscalco
...rico Riccardino
Patrizia Franceschina
Angelo Gerbino
Gabriele Borasi
Sergio Mulder
Francesco Serra
Silvia Lazzarotto
Carlo Alberto Demichelis
Franca Acuto
Corrado Fioravanti
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Gianluca Pulieri
...a Salustri
...i Gallo
Eleonora Guiotto
Fabiola Anna Quintavalle
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Pierluigi Carangelo
Marilena Garis
Nuria Abella Mendez
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Stefania Comisso
Monica Faia
Giuseppe Vitillo
Maria Antonella Incardona
Cristina Biggi
Dora Papagno

Jacobacci & Partners

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DR. ALESSANDRA ORI
VIA QUATTRO VILLE 251/1
41100 MODENA MO

- by *registered mail* -
Return receipt requested

Torino, January 5, 2006
Our ref.: E053638 - PC451PR (please quote) BEE-fl
Fresenius ref.: F02/04IT-I08

International patent application No. PCT/EP2003/009174 filed August 19, 2003
FRESENIUS HEMOCARE ITALIA SRL
FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS
(ITALY No. TO2002A000736)

Dear Dr. Ori,

Subsequent to our letter of February 16, 2005, in which we enclosed the declaration/power of attorney and assignment forms to be signed by you in order to complete the filing of the national phase corresponding to the above cited International patent application in the USA; and subsequent to your letter refusing to sign said documents dated March 14, 2005, our U.S. associate counsel has requested that we forward the enclosed copy of the complete U.S. application to you, together with another declaration/power of attorney and assignment documents.

We again request that you review the application and execute the declaration/power of attorney and assignment documents and return them to us so that we may complete our filing of this application in the USA.

We ask your prompt attention to this request.

Yours faithfully,
JACOBACCI & PARTNERS

P. Rambelli

Encl.: as above

Return receipt E053638/PC415PR/BEE/fl

X Registered mail No. 11681310239 4

Dispatching date 10/01/2006 From Post Office of Turin

Addressee Dr. ALESSANDRA ORI

Address VIA QUATTRO VILLE 251/1

Zip code 41100 City MODENA MO

X on behalf of

signed (illegible)
complete signature of addressee

26-01-2006
Date

signed (illegible)
signature of the person in charge of the dispatch

Stamp of the office in charge of the dispatch: Post Office of VILLANOVA SAN PANCRAZIO (MO) 26-01-2006

Italian Post Offices

Return receipt

To be returned to JACOBACCI & PARTNERS S.p.A.
Corso Emilia 8
10152 TORINO

Dr. Alessandra Ori
Via Quattro Ville, 251/1 – 41010 Modena

Racc. A.R. J&P Jacobacci & Partners
Corso Emilia, 8
10152 Torino
Torino Centro P.O. Box 321
10121 Torino

Modena, 14 Febbraio 2006

Vs. rif.: E053638 – PC451PR BEE-fl

Oggetto: Vs. richiesta mia firma su moduli di procura necessaria per l'estensione all' estero della domanda italiana n° TO2002A000736 depositata il 21 Agosto 2002 " FILTRO PER LEUCOCITI E SUO IMPIEGO PER L'IMPOVERIMENTO DI PRODOTTI DEL SANGUE ... " a nome di Fresenius HemoCare Italia S.r.l.

La presente per informarVi che NON intendo firmare i moduli di procura citati in oggetto che pertanto Vi restituisco in allegato.

Cordiali saluti.

Alessandra Ori

All.: moduli di procura in oggetto

PCa5-PRINS

DECLARATION AND POWER OF ATTORNEY U.S.A.

ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION;
NON PRIORITY; OR PROVISIONAL APPLICATIONS

FOR ATTORNEYS' USE ONLY

ATTORNEYS' DOCKET NO.

101 As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

"Filter for the depletion of leukocytes from blood products"

102 the specification of which:

☐ is attached hereto OR ☒ was filed on: August 19, 2003 as United States Application Number or PCT International application Serial No. PCT/EP2003/009174

and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) or (f), or 365(b) of any foreign application(s) for patent or inventor's or plant breeder's rights certificate, or under 35 U.S.C. 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's or plant breeder's rights certificate(s) having a filing date before that of the application on which priority is claimed:

103

Prior Foreign Application(s) (Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed
T02002A000736	Italy	21/08/2002	☒ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

104 I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105 I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status: patented, pending, abandoned)

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I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201*	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
		X
DATE	DATE	DATE

☐ Additional inventors are named on separately numbered sheets attached hereto.

Firma

PCL5d PRINTS

UNITED STATES OF AMERICA - ASSIGNMENT

(1-6) Insert Name(s) of Inventors

-1 Giorgio MARI

-2 Paolo VERRI

-3 Alessandra ORI

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-5 and

-6

In consideration of the sum of one dollar ($1.00), and other good and valuable considerations paid to each of the undersigned, the receipt and sufficiency of which are hereby acknowledged, the undersigned agree(s) to assign, transfer and set over to

-7 Insert Name of Assignee

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-8 of Via Santi 293, I-41032 CAVEZZO (Modena) Italy

-9 Insert Legal Entity and State or Country (e.g., a corporation or citizen of Japan)

-9 a Corporation of Italy

(hereinafter designated as the Assignee) the entire right, title and interest for the United States, its territories, dependencies and possessions, in the invention known as

-10 Insert Identification of Invention, such as Title, Case Number or Foreign Application Number

-10 "Filter for the depletion of leukocytes from blood products"

for which the undersigned has (have) executed an application for patent in the United States of America

-11 Insert Date of signing of Application, or filing date and Serial No., if known

-11 Said application having been executed/filed on _____ (and assigned Serial No. _____

1) The undersigned agree(s) to execute all papers necessary in connection with this application and any continuing or divisional applications and also to execute separate assignments in connection with such applications as the Assignee may deem necessary or expedient.

2) The undersigned agree(s) to execute all papers necessary in connection with any interference which may be declared concerning this or any continuing or divisional applications thereof and to cooperate with the Assignee in every way possible in obtaining evidence and going forward with such interference.

3) The undersigned agree(s) to execute all papers and documents and perform any act which may be necessary in connection with claims or provisions of the International Union for Protection of Industrial Property or similar agreements.

4) The undersigned agree(s) to perform all affirmative acts which may be necessary to obtain a grant of a valid United States patent to the assignee.

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6) Assignor hereby further assigns to Assignee all claims and causes of action for infringement of the patent rights assigned herein, including the right to sue for, and collect damages for, any and all acts of past and future infringement.

7) The undersigned hereby grant(s) the law firm of **Jacobson Holman PLLC**, 400 Seventh Street, N.W., Washington, D.C. 20004, the power to insert on this assignment any further identification which may be necessary or desirable in order to comply with the rules of the United States Patent and Trademark Office for recordation of this document.

In witness whereof, executed by the undersigned on the date(s) opposite the undersigned name(s).

Date	Name of Inventor			
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_____	_____	typed name	_____	signature (SEAL)
_____	_____	typed name	_____	signature (SEAL)

This assignment should preferably be signed before a United States Consul if signed abroad, or a Notary Public if domestically signed. If not, then the execution by the inventor(s) should be witnessed by at least two witnesses who sign here:

☐ Additional inventors' names and signatures on a separate sheet.

Witness _____

Witness _____

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JH PLLC 4/03

IN THE SPECIFICATION

On page 1, immediately following the title, please insert the following sentence:

This is a nationalization of PCT/EP03/009174 filed August 19, 2003 and published in English.

IN THE CLAIMS

Claim 1 (original): A filter device for the depletion of the leukocyte content from blood products comprising a housing with an inlet and an outlet port and, within said housing, at least two porous elements adapted for removing leukocytes, each porous element comprising one or more layers of filtering material, wherein said at least two porous elements have a different hydrophilicity, characterized in that the said porous elements are arranged in the filter device so that the first element has a higher hydrophilicity than the successive filter element(s) in the direction of flow, from inlet to outlet, of the blood product though the filter device.

Claim 2 (original): A filter device according to claim 1 comprising more than two filter elements for leukocyte depletion, characterized in that any given filter element has a higher hydrophilicity than its successive filter element in the direction of flow of the blood product through the filter device from inlet to outlet.

Claim 3 (currently amended): A filter device according to claim 1 ~~or 2~~ wherein each porous element comprises at least two adjacent layers of filtering material.

Claim 4 (original): A filter device according to claim 3, wherein said at least two layers of filtering material are made of the same material having the same hydrophilicity properties.

Claim 5 (currently amended): A filter device according to claim 3 ~~or 4~~, wherein said at least two layers have a decreasing pore size from inlet to outlet.

Claim 6 (currently amended): A filter device according to claim 1 ~~any of claims 1 to 5~~, wherein any given porous element is made of a filtering material having a pore size higher than the pore size of its successive porous element.

Claim 7 (currently amended): A filter device according to claim 1 ~~any of claims 1 to 6~~, wherein said porous elements are made of fibers of a polymeric material selected from the group consisting of polyester, polyolefines, polyamide and polyester, polyolefines or polyamides coated with a hydrophilic polymer and mixtures of said fibers.

Claim 8 (original): A filter device according to claim 7, wherein said hydrophilic polymer is selected from the group consisting of hydrophilic acrylic polymers or copolymers and hydrophilic polyurethane.

Claim 9 (original): A filter device including at least a first porous element made of layers of polybutylenterephthalate fibers coated with a hydrophilic polymer or copolymer and a second porous element made of uncoated polybutylenterephthalate or polypropylene layers.

Claim 10 (currently amended): A filter device according to claim 1 ~~any of the preceding claims~~ comprising two or more porous elements for leukocyte depletion made of one or more layers of filtering material, wherein said porous elements are arranged in the filter device according to a decreasing value of the CST or CWST of the constituting material, from inlet to outlet.

Claim 11 (currently amended): A filter device according to claim 1 ~~any of the preceding claims~~ wherein the difference between the hydrophilicity of the inlet porous element and the final outlet

porous element, as measured by the value of the CST or CWST of the constituting material is of at least 10 dyn/cm.

Claim 12 (currently amended): A filter device according to claim 1 ~~any of the preceding claims~~, wherein the difference between the hydrophilicity of the inlet porous element and the final outlet porous element, as measured by the value of the CST or CWST of the constituting material is of from 10 to 20 dyn/cm.

Claim 13 (currently amended): A filter device according to claim 1 ~~any of the preceding claims~~ wherein the first inlet porous element is made of material having a hydrophilicity as measured by the CST or CWST of the constituting material higher than 63 dyn/cm.

Claim 14 (currently amended): A filter device according to claim 1 ~~any of claim 1 to 8~~ comprising within said housing one or more additional filter elements of any hydrophilicity which are not adapted for leukocyte removal (e.g. gel filtration elements or microaggregate filtration elements).

Claim 15 (original): A filter device according to claim 14 wherein said filter elements not adapted for leukocyte removal are located closer to the inlet than said elements adapted for leukocyte removal.

Claim 16 (currently amended): A blood bag device for the separation of blood into leukocyte depleted blood components comprising at least a first bag connected, in fluid flow communication with a second bag through a leukocyte filter device according to claim 1 ~~any of claims 1 to 13~~.

Claim 17 (currently amended): A method for the leukocyte depletion of blood products comprising feeding said blood product through a

filter device according to claim 1 ~~any of claims 1 to 14~~.

Claim 18 (original): A method according to claim 17, wherein said blood product is selected from the group consisting of whole blood, platelet-rich plasma, packed red cells, platelet concentrate and plasma.

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Declarations under Rule 4.17:
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS

(57) Abstract: A filter device for the depletion of the leukocyte content from blood products including two or more porous elements each made of one or more layers or filtering materials, wherein said porous elements are arranged in the filter device according to decreasing hydrophilicity, from inlet to outlet, of the filtering material constituting said elements.

WO 2004/018078 A1

FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS

The present invention relates to a filter device for the depletion of the leukocyte content from blood products such as whole blood and/or blood components.

More particularly, the invention relates to a leukocyte filter device adapted for use in the blood bag systems which are conventionally used for the separation of whole blood into leukocyte depleted hemocomponents.

Blood bag systems are known e.g. from US-4,596,657, EP-A-0 556 303 and EP-A-0 879 608.

US-4,596,657 describes a blood bag system including a primary bag which is connected by means of flexible hose lines to a first and a second satellite bag; a filtering means is integrally disposed between the primary bag and one satellite bag to remove platelets and leukocytes from a mixture of a red cell concentrate and additive solution which is passed through the filtering means from the primary bag to the said satellite bag.

EP-A-0 556 303 and US-5,100,564 describe a blood collection and processing system for preparing, from donated whole blood, platelet-rich plasma (PRP), packed red cells (PRC), platelet concentrate (PC) and plasma; in the described system, PRP is leukocyte depleted by interposing in the conduit between a blood collection bag and a first satellite bag a filter assembly for depleting leukocytes from PRP; in the same way, PRC is leukocyte depleted by interposing between the blood collection bag and a second satellite bag a second

filter assembly for removing leukocytes from PRC.

EP-A-0 879 680 describes a blood bag system for separating blood into blood components wherein leukocyte-free PRC is prepared by passing erythrocytes resuspended in an additive agent through a leukocyte filter.

The leukocyte filters, to which the present invention relates, typically comprise a housing with inlet and outlet ports and at least a porous element, within the housing, interposed between the inlet and outlet port. The said porous element usually consists of a web or mat which may be formed by one or more layers of filtering material, typically a non-woven fabric, which may or may not be bonded to each other.

According to the prior art, the porous elements can be produced from any material compatible with blood which is capable of forming fibers including natural or synthetic fibers. The preferred materials are synthetic polymers such as particularly polyolefines, polyesters, and polyamide; polybutylenterephthalate (PBT) is currently considered as a preferred polymer.

A parameter which is considered in the design of the porous elements is the critical surface tension (CST) of the employed material. The CST of a surface is a measure of the repellent properties of that surface; it is the maximum surface tension for a liquid that has a contact angle $\theta = 0°$. CST cannot be measured directly on textile yarns that are complex bundles of twisted fibers; however, the CST for yarns may approximate that for chemically related plane surfaces.

With reference to the materials used in filters for leukocyte

depletion, EP-A-0 313 348 describes an empirical method for measuring the critical surface tension of a porous medium, therein defined as "Critical Wetting Surface Tension" (CWST). According to said method, the CWST of a porous medium is determined by individually applying to its surface, preferably drop wise, a series of liquids with a surface tension varying by 2 to 4 dyn/cm (mN/m) and observing the absorption and non-absorption of each liquid. The CWST of the porous medium in units of dyn/cm is defined as the mean value of the surface tension of the liquid which is absorbed and that of a liquid of neighboring surface tension which is not absorbed. Liquids with surface tension lower than the CWST of a porous medium or the CST of a given material will spontaneously wet the medium or material on contact. With reference to water (surface tension 72 dyn/cm), materials having a CST lower than the surface tension of water, will not be wetted. The CST of a material can therefore be taken as measure of the hydrophilicity of the material itself; the higher the CST or CWST, the higher is the hydrophylicity of the material.

EP-A-0 313 348 describes a device for the depletion of the leukocyte content of a blood product comprising a first porous element for removing gels, a second porous element for removing micro-aggregates and a third element for removing leukocytes, wherein at least the third element has been modified to a critical wetting surface tension in the range of from greater than 53 dyn/cm to less than 90 dyn/cm and wherein each successive element, from inlet to outlet, has a smaller pore diameter than that preceding it.

In these filters, gels and micro-aggregates are removed before filtering leukocytes. In the working examples of EP-A-0 313 348 the device comprises a first layer for gel filtra-

tion made of acrylic bonded needle punched PET, with a CWST of 50 and a plurality of additional layers for micro-aggregate removal and leukocyte adsorption having increased CWST which are typically made of melt-blown PBT which is surface grafted to increase its CWST. When the final porous element for leukocyte removal is made of a plurality of layers, these are usually made of the same material.

US-5,580,465 describes a method for preparing platelets by passing platelet-rich plasma (PRP) through a filter comprising a porous medium with a CWST of at least 70 dyn/cm under conditions sufficient to remove about 99.99% of the leukocytes from the PRP. From this document it can be derived that the increased hydrophylicity of the modified PBT filter element is enhancing the recovery of thrombocytes.

US-4,963,260 describes a liquid filtering device for separating leukocytes comprising a first filter element and a second filter element in a position downstream of the first one, wherein the second filter element is made of a material having a larger filtration resistance than the first filter element; filter resistance can be increased by decreasing pore size which also regulates the liquid pressure.

In view of the available prior art there is still a need for leukocyte filter devices having improved efficiency in leukocyte removal and better overall performance.

To this end, the present invention provides a filter device for the depletion of the leukocyte content from blood products comprising a housing with an inlet and an outlet port and, within said housing, at least two porous elements, adapted for removing leukocytes, each porous element compris-

ing one or more layers of filtering material, wherein said at least two porous elements have different hydrophylicity, characterized in that the said porous elements are arranged in the filter device so that the first element has a higher hydrophylicity than the successive filter element(s) in the direction of flow, from inlet to outlet, of the blood product through the filter device.

Further characterizing features of the filter device according to the invention are defined in the appended claims.

As noted before, the CST of the filtering material or the CWST of a porous fabric made of said material can be taken as a measure of the hydrophylicity of the employed material, whereby a higher hydrophylicity corresponds to a higher CST or CWST.

In a preferred embodiment of the invention, the filter device comprises more than two porous elements and the hydrophylicity (CST or CWST) of any given element is higher than the hydrophylicity of its successive element in the direction of flow from inlet to outlet, so as to establish a decreasing hydrophylicity profile (negative gradient).

Each porous element for leukocyte depletion may be comprised of one or more layers of adjacent filtering sheet material, which layers may optionally be bonded to each other. When a porous element is made of two or more layers, these will usually be made of the same filtering material having the same filtering and hydrophilicity properties. However, the said filtering layers may have different pore size, such as optionally a decreasing pore size from inlet to outlet, as suggested by the prior art.

Also, successive porous elements from inlet to outlet may have a different pore size such as optionally a decreasing pore size.

The filter according to the invention may include within the filter housing upstream of the first porous element for leukocyte depletion, one or more porous elements specifically adapted for gel or micro-aggregate removal from the blood product.

The constructive principle underlying the invention is not intended to be limited to any specific filtering material and, in principle, any commercially available filtering material which is compatible with blood can be used. The filtering material is however preferably based on polyesters, such as PET or PBT or on more hydrophobic polymers such as polyolefines, particularly polypropylene, or polyamide.

The said hydrophobic polymer material can be rendered more hydrophilic by coating the fibers of the material with a more hydrophilic polymer such as particularly hydrophilic acrylic polymers or copolymers or hydrophilic polyurethane. The polymeric material can also be rendered more hydrophilic by surface grafting the polymeric material, particularly PBT, with compounds containing an ethylenically unsaturated group, such as an acrylic moiety combined with hydroxyl groups or methylacrylate or methylmethacrylate and combinations thereof, as described in EP-A-0 313 348. The layers of the filtering elements are usually made of a non-woven fabric obtained from fibers of the polymeric materials; however, also porous membranes or sintered porous media could be used in principle.

The absolute value of the CWST of the inlet filtering layer

and successive layers can be selected in a wide range, according to the principles known in the art and depending upon the blood product (whole blood or other hemocomponents) which is to be leukocyte depleted by passing through the filter device. Preferably, the CWST of the inlet layer is of at least 53 dyn/cm (pure PBT) and more preferably of at least 63 dyn/cm.

The minimum and maximum wettability (CWST) difference between the first and last filter layer from inlet to outlet may vary in a wide range and may depend upon the distance between the bag containing the blood product and the layer, that is on the pressure generated by the column of liquid which is available for driving the blood product through the filter.

A preferred minimum wettability (CWST) difference is of about 10 dyn/cm, particularly when the inlet layer has a CWST of about 63 and independently from the distance between the bag and the filter device. A preferred maximum wettability (CWST) difference is of about 20 dyn/cm when the CWST of the outlet layer has a value of 53 dyn/cm (pure PBT).

As stated before, a preferred embodiment of the invention contemplates the use of a plurality of filter elements each consisting of a set of filter layers, such as particularly from 3 to 8 sets each comprising a plurality of layers, such as preferably from 2 to 50 layers. The difference in the wettability (CWST) of adjacent sets of layers can be in the range of from 2 to 50 dyn/cm.

The subject matter of the invention also includes a blood bag device including at least a primary and a satellite bag, connected by a flexible conduit wherein a filter device accord-

ing to the invention is interposed in the flexible conduit for leukocyte depletion.

In a preferred embodiment of such a device the distance between the primary bag and the filter element is 20 to 80 cm, more preferably between 30 and 50 cm.

A further subject of the invention is the use of the described filter device for leukocyte depletion of blood products. The blood products include whole blood and other hemocomponents such as particularly platelet-rich plasma (PRP), packed red cells (PRC), platelet concentrate (PC) and plasma (PL).

In order to allow the user to properly set up the filter device of the invention in the blood bag system, the housing of the filter device may include appropriate indicia allowing to identify the inlet and outlet ports so that the filter device is mounted according to the appropriate negative hydrophilicity gradient from inlet to outlet.

It has been found that in the filter according to the invention the first set (or filter element) of more hydrophilic layers is easily wetted by the liquid and therefore the liquid pressure is distributed evenly on the following more hydrophobic layers. With this filter set-up regional pressure differences because of gas bubbles attached to the surface of the filter can be prevented, which decreases the risk of micro-ruptures in the filter.

The described arrangement improves the air elimination from the filter material, avoiding blood flow channeling, leading to a better leukocyte removal efficiency; moreover, by better

exploiting the whole filtering material, its quantity can be reduced with consequent reduced cell loss.

A further advantage of a filtration system containing described filter element is that due to the improved wettability of the inlet layer the needed priming pressure as well as the priming time of the filter is reduced.

For the same reason the gravity pressure head which is needed for the efficient filtration of the liquid can be reduced. Therefore the distance needed between the primary bag and the filter element is smaller which is saving both space and tubing material.

In contrast to a filter with an inlet layer of 53 dyn/cm for which a distance to the primary bag of at least 80 cm is needed, for a filter with an inlet layer of 68 dyn/cm a distance of 30 cm is sufficient for efficient filtration of blood or blood components.

Further advantages and features of the filter device of the invention will be apparent from the following non limiting working examples.

Example 1

The filter device consists of 39 layers of PBT (50 g/m^2, CWST 53 dyn/cm) and one layer of polypropylene (10 g/m^2, CWST 33 dyn/cm). The filter device is used with a conventional blood bag system and is mounted in the flexible conduit connecting the primary bag to a first satellite bag at a distance of 80 cm from the primary bag. Whole blood is filtered through the filter device and the following features and parameters are

obtained:
Filter priming time: 3 min.
Filtration time of one whole blood unit (about 450cm^3): 28 min.
Blood volume recovery: 92%
Residual white blood cells: 200,000/unit

By way of comparison, a filter device was used without the polypropylene layer which was replaced by a PBT layer so as to achieve the same filter volume; the white blood cell contamination was found to be 900,000/unit.

Example 2

Use is made of a filter consisting of 35 layers of coated PBT (50g/m^2) wettable with a 68 dyn/cm liquid and 5 layers of uncoated PBT (50g/m^2), CWST 53 dyn/cm; the filter was placed at the distance from the primary bag of 30 cm.
Filter priming time: 1,5 min.
Filtration time of one whole blood unit (about 450 cm^3): 20 min.
Blood volume recovery: 92%
Residual white blood cells: 100,000/unit

For a filter with a CWST of 53 dyn/cm without the hydrophilicity gradient the white blood cell contamination was found to be 1,100,000/unit.

Example 3

Use is made of a filter consisting of 5 packages of 5 layers each of coated and uncoated PBT which were stacked together as follows:
First set: 63 dyn/cm

Second set: 61 dyn/cm
Third set: 59 dyn/cm
Fourth set: 55 dyn/cm
Fifth set: 52 dyn/cm
Distance bag/filter: 30 cm
Filter priming time: 1 min.
Filtration time of one whole blood unit (about 450 cm^3): 15 min.
Blood volume recovery: 92%
Residual white blood cells: 50,000/unit.

CLAIMS

1. A filter device for the depletion of the leukocyte content from blood products comprising a housing with an inlet and an outlet port and, within said housing, at least two porous elements adapted for removing leukocytes, each porous element comprising one or more layers of filtering material, wherein said at least two porous elements have a different hydrophilicity, characterized in that the said porous elements are arranged in the filter device so that the first element has a higher hydrophilicity than the successive filter element(s) in the direction of flow, from inlet to outlet, of the blood product though the filter device.

2. A filter device according to claim 1 comprising more than two filter elements for leukocyte depletion, characterized in that any given filter element has a higher hydrophilicity than its successive filter element in the direction of flow of the blood product through the filter device from inlet to outlet.

3. A filter device according to claim 1 or 2 wherein each porous element comprises at least two adjacent layers of filtering material.

4. A filter device according to claim 3, wherein said at least two layers of filtering material are made of the same material having the same hydrophilicity properties.

5. A filter device according to claim 3 or 4, wherein said at least two layers have a decreasing pore size from inlet to outlet.

6. A filter device according to any of claims 1 to 5, wherein any given porous element is made of a filtering material having a pore size higher than the pore size of its successive porous element.

7. A filter device according to any of claims 1 to 6, wherein said porous elements are made of fibers of a polymeric material selected from the group consisting of polyester, polyolefines, polyamide and polyester, polyolefines or polyamides coated with a hydrophilic polymer and mixtures of said fibers.

8. A filter device according to claim 7, wherein said hydrophilic polymer is selected from the group consisting of hydrophilic acrylic polymers or copolymers and hydrophilic polyurethane.

9. A filter device including at least a first porous element made of layers of polybutylenterephthalate fibers coated with a hydrophilic polymer or copolymer and a second porous element made of uncoated polybutylenterephthalate or polypropylene layers.

10. A filter device according to any of the preceding claims comprising two or more porous elements for leukocyte depletion made of one or more layers of filtering material, wherein said porous elements are arranged in the filter device according to a decreasing value of the CST or CWST of the constituting material, from inlet to outlet.

11. A filter device according to any of the preceding claims wherein the difference between the hydrophilicity of the inlet porous element and the final outlet porous element, as

measured by the value of the CST or CWST of the constituting material is of at least 10 dyn/cm.

12. A filter device according to any of the preceding claims, wherein the difference between the hydrophilicity of the inlet porous element and the final outlet porous element, as measured by the value of the CST or CWST of the constituting material is of from 10 to 20 dyn/cm.

13. A filter device according to any of the preceding claims wherein the first inlet porous element is made of material having a hydrophilicity as measured by the CST or CWST of the constituting material higher than 63 dyn/cm.

14. A filter device according to any of claim 1 to 8 comprising within said housing one or more additional filter elements of any hydrophilicity which are not adapted for leukocyte removal (e.g. gel filtration elements or microaggregate filtration elements).

15. A filter device according to claim 14 wherein said filter elements not adapted for leukocyte removal are located closer to the inlet than said elements adapted for leukocyte removal.

16. A blood bag device for the separation of blood into leukocyte depleted blood components comprising at least a first bag connected, in fluid flow communication with a second bag through a leukocyte filter device according to any of claims 1 to 13.

17. A method for the leukocyte depletion of blood products comprising feeding said blood product through a filter device

according to any of claims 1 to 14.

18. A method according to claim 17, wherein said blood product is selected from the group consisting of whole blood, platelet-rich plasma, packed red cells, platelet concentrate and plasma.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09174

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01D39/16 A61M1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01D A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 20053 A (PALL CORP ;SELMAN BYRON (US); BORMANN THOMAS J (US); DELGIACCO GER) 13 April 2000 (2000-04-13) examples	1,2,7,8, 10
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A	EP 1 093 823 A (MACO PHARMA) 25 April 2001 (2001-04-25) claims 1-9	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 December 2003	10/12/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Plaka, T

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09174

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09174

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- by returned registered mail -

J&P Jacobacci & Partners
Corso Emilia, 8
10152 Torino
Torino Centro P.O. Box 321
10121 Torino

Modena, February 14, 2006

Your ref.: E053638 - PC451PR BEE-fl

Re: Your request for my signature on the power of attorney forms required for the foreign filing of the Italian patent application No. TO2002A000736 filed August 21, 2002 "FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS" in the name of FRESENIUS HEMOCARE ITALIA SRL

I hereby inform you that I DO NOT intend to sign the forms in re; therefore I am sending back to you the above forms.

Yours faithfully.

Alessandra Ori

signed (illegible)

Encl.: power of attorney forms in re

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TORINO | MILANO | PADOVA | ROMA | BRESCIA | GENEVE | MADRID | ALICANTE

Torino, February 23, 2006
Our ref.: E059646 - PC451PR/US

U.S.A. - Patent Application No. 10/525044 of August 19, 2003
corresponding to International patent application No. PCT/EP2003/009174
FRESENIUS HEMOCARE ITALIA SRL
FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS
(ITALY No. TO2002A000736)

I, Paolo Rambelli, Patent attorney at Jacobacci & Partners S.p.A., Corso Emilia 8, I-10152 TORINO (Italy) hereby state that on February 20, 2006 we received another letter signed by Ms. Alessandra ORI dated February 14, 2006, reasserting her refusal to sign the declaration/power of attorney relating to the above mentioned US patent application (as already done in her letter of March 14, 2005).

Paolo RAMBELLI

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- by air courier

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FEB 28 2006
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20004-2201 WASHINGTON D.C.
U.S.A.

Turin, February 23, 2006
Our ref. : E059646 PC451PR/US (please always quote) BEE-fl
Your ref.: 13380/P70417US0

U.S.A. - Patent Application No. 525044
corresponding to International Application No. PCT/EP2003/009174 of August 19, 2003
FRESENIUS HEMOCARE ITALIA S.r.l.
FILTER FOR THE DEPLETION OF LEUKOCYTES FROM BLOOD PRODUCTS

Dear Sirs:

With reference to your letter of February 13, 2006, please find enclosed herewith an additional refusal letter sent by Ms. Ori, returning the documents which were sent to her on January 5, 2006.

Also enclosed please find the English translation of Ms. Ori's refusal letter and our letter stating the specific date of receipt of said refusal letter at our firm.

Please acknowledge receipt of the original documents.

Yours faithfully,
JACOBACCI & PARTNERS

P. Rambelli

Encl.: as above

ACKNOWLEDGED
WITH THANKS
JACOBSON HOLMAN PLLC
DATE 2/28/06